

## ABSTRACT

The present invention is to provide a non-human animal model non-responsive especially to endotoxin being a Gram-negative bacteria cell wall fraction, which is useful to elucidate the function of TIR domain-containing TRIF-related adaptor molecule (TRAM); and a method for screening substances promoting or suppressing responses to ligands recognized by TLR4 with the use of the non-human animal model non-responsive to endotoxin; and the like. Mice non-responsive to the endotoxin wherein a part or a whole of Tram genes on their chromosome are deleted, the function to express TRAM which is expressed in wild-types is lacked, and the responsiveness to ligands recognized by TLR4 is specifically impaired; is used for screening substances promoting or suppressing responses to ligands recognized by TLR4.